UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,223	06/29/2005	Heinz Schneider	09600-00031-US	9409

23416 7590 04/19/2007

CONNOLLY BOVE LODGE & HUTZ, LLP
P O BOX 2207
WILMINGTON, DE 19899

EXAMINER	
MCCORMICK, MELENIE LEE	
ART UNIT	**PAPER NUMBER**
1655	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,223	SCHNEIDER, HEINZ	
	Examiner	Art Unit	
	Melenie McCormick	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-10,16 and 18-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-10,16, and 18-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/23/2007 has been entered.

Claims 3-10, 16, and 18-25 are presented for examination on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-10 and 16, 18-21 and 23-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition and a method for reducing the risk of postoperative ischemia reperfusion injury, does not reasonably provide enablement for a composition and a method which is effective in reducing the risk of any and all postoperative complications, as instantly claimed. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are directed to a composition comprising green tea extract and at least one NO donor which is a substrate of NO synthetase, and/or one precursor of this NO donor, wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine and a method for reducing the risk of postoperative complication comprising the step of administering a composition which comprises green tea extract and at least one NO donor which is a substrate of NO synthetase, and/ or one precursor of this NO donor, wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine .

While Applicant has reasonably demonstrated the instantly claimed composition and method may be enabling for reducing the risk of postoperative ischemia reperfusion (see e.g. Specification- pgs 11-12), Applicant has not demonstrated that the instantly claimed composition and method are able to reduce the risk of all possible post-operative complications, which are encompassed by the instant claims.

As evidenced by Kerr et al., one possible postoperative complication is hypercapnia (see e.g. page 588, last para). Such a postoperative complication is encompassed by the instant claims, which read on any and all postoperative complications.

Nowhere in the specification as originally filed does Applicant demonstrate that the claim-designated composition comprising green tea extract and at least one NO donor which is a substrate of NO synthetase, and/or one precursor of this NO donor,

wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine and method for reducing the risk of postoperative complication comprising the step of administering a composition which comprises green tea extract and at least one NO donor which is a substrate of NO synthetase, and/ or one precursor of this NO donor, wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine is effective in reducing the risk of hypercapnia.

Thus, while Applicant has reasonably demonstrated a composition and method enabling reducing the risk of postoperative ischemia reperfusion following selected surgical procedures, Applicant has not demonstrated the claim-designated composition and method are effective in reducing the risk of all postoperative complications (including, for example, hypercapnia). Therefore, it would require undue experimentation without a reasonable expectation of success in order to determine the efficacy of the claim-designated composition and method in reducing the risk of any and all postoperative complications, as broadly claimed by Applicant.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 depends from claim 16 and recites the limitation "wherein component b) is arginine or an arginine precursor in the form of a di- or tripeptide" in lines 1-2. It is not clear how component b can be arginine or an arginine precursor when claim 16 (from which claim 20 depends) does not include arginine or and arginine precursor in the group which component b is selected from.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-10, 16, 18-19, and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inanami et al. (Free Radic Res), Schnieider et al. (US 6,656,608), Sherrat et al. (US 6,423,349), and Schnieder et al. (5,902,829).

A formulation for gastrointestinal administration to a surgical patient before a surgical procedures to reduce the risk of postoperative complications or to avert such a risk comprising a composition comprising green tea extract and at least one NO donor which is a substrate of NO synthetase, and or one precursor of this NO donor, wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine is claimed. A method of averting or reducing the risk of postoperative

complications comprising the step of gastrointestinally administering to a surgical patient a composition comprising green tea extract and at least one NO donor which is a substrate of NO synthetase, and or one precursor of this NO donor, wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine is also claimed.

Inanami et al. beneficially teach the protective effects of the green tea polyphenol (-) catechin against damage in the brain caused by ischemia in gerbils. Inanami et al. further teach that the compound is intended to be orally (gastrointestinally) administered prior to a reperfusion event (surgery)- see entire document including abstract and methods. Please note that theanine is one of the predominant amino acids present in green tea, and would intrinsically be present in an extract of green tea. Inanami et al. do not expressly teach that the composition further comprises glycine or at least one NO donor which is a substrate of NO synthetase.

Schneider et al. '608 beneficially teach that glycine is useful in protecting against damage caused by ischemia reperfusion. Schneider et al. further beneficially teach that a composition comprising glycine is intended to be administered orally (see e.g. col 5 line 66-col 6 line 2). Schneider et al. also further beneficially teach that the composition is intended as a pre-operative treatment (see e.g. col. 6 lines 21-23).

Sherratt et al. beneficially teach a composition and a method of administering a composition to patients prior to elective surgery in order to protect against ishchemia reperfusion (see e.g. col 4, lines 35-45 and col 5, lines 1-3 and 42-45). Sherratt et al.

further teach that nitroglycerin is useful in this method and composition to decrease reperfusion injury (see e.g. col 4, lines 53-66). It is further disclosed by Sherratt et al. that reperfusion injury is attenuated by administration of free radical scavengers (see e.g. col 5, lines 5-7). Sherratt et al. further teach that glutamine is a free radical scavenger and that glutamine is administered to patients in order to promote the recovery of elective surgery (see e.g. col 5, lines 22-37 and lines 45-63 and claim 1). Sherrat et al. further teach that the composition is administered to patients prior to elective surgery, particularly for two days prior to the surgery (see e.g. claim 9) and that the administration is oral or via a feeding tube (see e.g. col 10, lines 8-10).

Schneider et al. '829 beneficially teach a composition and a method of administering the composition pre-operatively which reduces the risk of reperfusion injury in patients who undergo elective surgery (see e.g. col 1, lines 21-26). Schneider et al. further teach that L-arginine or a precursor of L-arginine is used for this purpose (see e.g. col 1, lines 27-34). It is further disclosed by Schneider et al. a precursor of L-arginine which may be used pre-operatively is glutamine (see e.g. col 1, lines 35-36 and claim 4).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the green tea extract taught by Inanami et al. and the glycine and glutamine taught by Schneider et al. '608 and Sherratt et al. and Schneider '829, respectively, to obtain a composition which would be useful for treating preoperative patients to reduce the risk of post operative complications (such as the oxidative injury caused by ischemia reperfusion). Since it is well known in the art that

the majority of damage resulting from ischemia reperfusion is related to oxidative stress, it would have been obvious to the skilled artisan and the skilled artisan would have been motivated and would have had a reasonable expectation of success in combining a well known antioxidant (green tea extract) with glutamine, especially since, as disclosed by Sherratt and Schneider et al. '829, glutamine is useful in protecting against of post operative reperfusion injury. Since it has also been shown that glycine may be useful as a treatment to protect against ischemia reperfusion (as disclosed by Schneider et al. '608), it would have been obvious to include this compound in composition which was to be used for the same purpose. Please note that the administration times taught by the instantly cited references would render obvious the instantly claimed administration which takes place less than twenty four hours prior to surgery because the references teach administration which *begins* before the surgery. Administration that begins any time prior to surgery and continues until the surgery would be taking place less than twenty four hours prior to surgery, as instantly claimed. The adjustment of particular conventional working conditions (e.g. administering the composition to a patient at a hour before or after surgery) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Claims 16 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inanami et al. (Free Radic Res), Schnieider et al. (US 6,656,608) and Jerkic et al. (Nephr Dial Trans), and further in view of Wu et al. (J. Nutr.).

Although difficult to interpret (see 112 2nd paragraph rejection above), the claims have been interpreted such that they are drawn to a formulation for gastrointestinal administration to a surgical patient before a surgical procedures to reduce the risk of postoperative complications or to avert such a risk comprising a composition comprising green tea extract and at least one NO donor which is a substrate of NO synthetase, ad or one precursor of this NO donor, wherein the NO donor and precursor are selected from arginine or an arginine precursor.

Inanami et al. and Schneider et al. are relied upon for the reasons set forth above.

Schneider et al. also disclose that the composition may additionally contain arginine (see e.g. claim 7).

Jerkic et al. beneficially teach the protective effects of L-arginine administration in rats prior to a surgical procedure which would result in reperfusion injury. Jerkic et al. further beneficially teach that L-arginine administration is through drinking water (gastrointestinal administration) prior to the surgery.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the green tea extract taught by Inanami et al. and the glycine and L-arginine taught by Schneider et al. and Jerkic et al., respectively, to obtain a composition which would be useful for treating preoperative patients to

reduce the risk of post operative complications (such as the oxidative injury caused by ischemia reperfusion). Since it is well known in the art that the majority of damage resulting from ischemia reperfusion is related to oxidative stress, it would have been obvious to the skilled artisan to combine a well known antioxidant (green tea extract) with L-arginine, especially since, as evidenced by Wu et al., L-arginine is notoriously well recognized in the art to be the main precursor of nitric oxide which is a known mediator of reperfusion (see Wu et al.-e.g., page ,2628). Since it has also been shown that glycine may be useful as a treatment to protect against ischemia reperfusion (as disclosed by Schneider et al.), it would have been obvious to include this compound in composition which was to be used for the same purpose. The adjustment of particular conventional working conditions (e.g. administering the composition to a patient at a certain time before or after surgery) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants argue that none of the previously cited references disclose or suggest the currently amended formulation and method. This is not wholly persuasive, however, as claim 20 still is still obvious over Inanami et al, Schnieider et al., Jerkic et al., and Wu et al. (see 103(a) rejection above. Further regarding Applicant's argument that the currently amended claims are not obvious over the previously cited references, it should be noted that while this may be true for some of the previously cited references, new references have been applied which, when combined, render obvious the instantly claimed invention.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melenie McCormick whose telephone number is (571) 272-8037. The examiner can normally be reached on M-F 7:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CHRISTOPHER R. TATE
PRIMARY EXAMINER